Zongertinib demonstrates promising efficacy in patients with HER2-mutant non-small cell lung cancer

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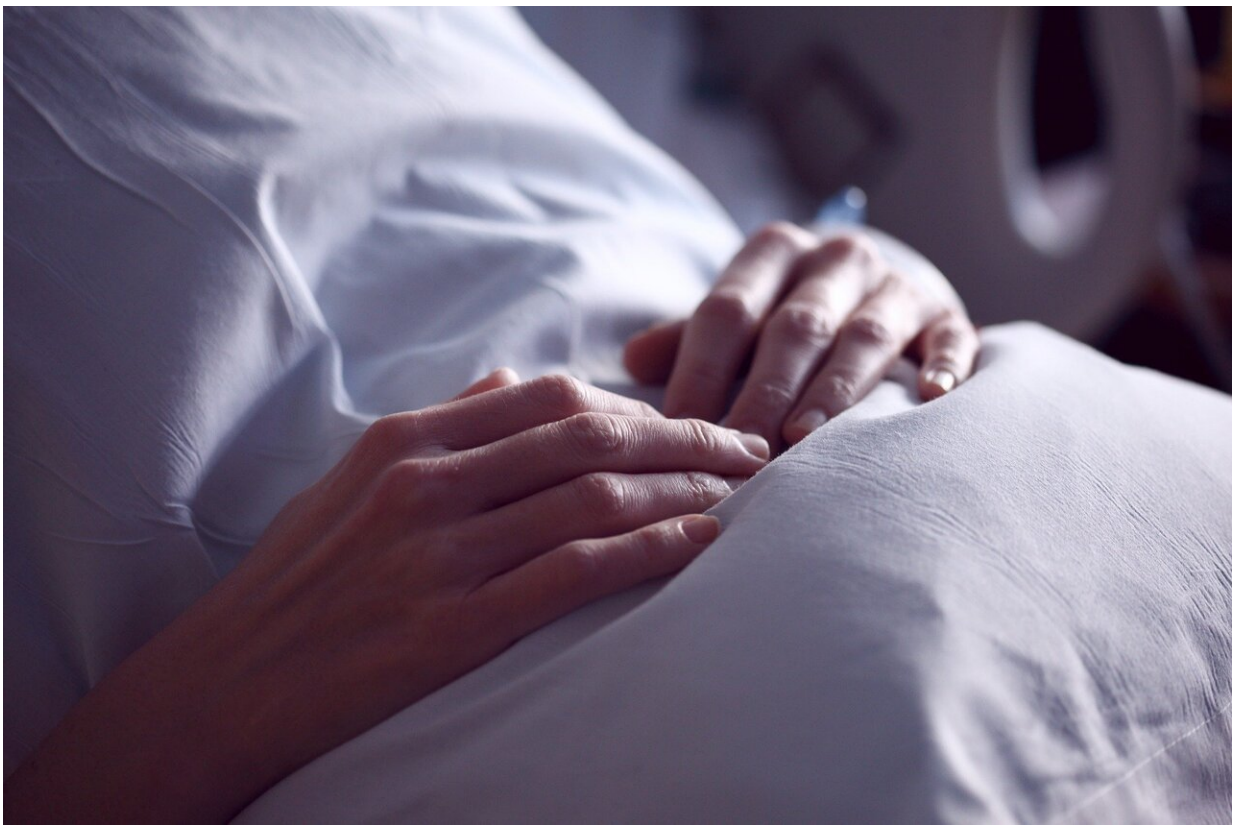

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The HER2-specific tyrosine kinase inhibitor zongertinib was well tolerated and demonstrated promising efficacy in patients with HER2

mutation-positive non-small cell lung cancer, meeting the primary endpoint of the Beamion LUNG-1 Phase Ib Cohort 1 study, according to research presented at the International Association for the Study of Lung Cancer 2024 World Conference on Lung Cancer.

Zongertinib is a novel, orally administered HER2-specific tyrosine kinase inhibitor designed to bind selectively and covalently to the tyrosine kinase domain of HER2, while sparing the wild-type epidermal growth factor receptor to limit EGFR-related adverse events.

In November 2023, the US Food and Drug Administration granted Fast Track Designation to zongertinib as an investigational treatment for patients with advanced/metastatic HER2 m+ NSCLC who had progressed following platinum-based therapy.

To further test zongertinib, Dr. Gerrina Ruiter, Department of Clinical Pharmacology and Thoracic Oncology, Netherlands Cancer Institute, Netherlands and colleagues at other sites, enrolled 132 patients in the Beamion LUNG-1 trial. Beamion LUNG-1 is an ongoing, Phase Ia/Ib, first-in-human, open-label study evaluating the safety and efficacy of zongertinib in patients with HER2 aberration-positive solid tumors (Phase Ia) and HER2 m+ NSCLC (Phase Ib).

Earlier Phase I data revealed that zongertinib achieved an overall response rate of 35.8% and a disease control rate of 94.3% in patients with HER2 m+ NSCLC, with manageable safety and limited EGFR-related adverse events.

Phase Ib of the study is recruiting patients with HER2 m+ advanced/metastatic NSCLC across five global cohorts. Cohort 1, focusing on previously treated HER2 TKDm+ NSCLC patients, initially randomized participants to receive 120 mg or 240 mg of zongertinib once daily.

The 120 mg daily dose was selected for further investigation based on interim analysis. The primary endpoint for Cohort 1 is overall response per RECIST version 1.1 by central independent review, with secondary endpoints including duration of response and progression-free survival.

As of May 2024, 132 patients have been treated in Phase Ib Cohort 1 with zongertinib at doses of 120 mg (n=75) and 240 mg (n=57) QD. The median age of patients was 62 years, with 57.6% being female. The median treatment duration was 7.6 months, and 87 patients (65.9%) were still receiving treatment at the time of data cut-off.

Adverse events were reported in 99.2% of patients, with the most common adverse effects being diarrhea (55.3% overall; 1.5% grade ≥3), rash (26.5% overall; 0% grade ≥3), and increases in alanine aminotransferase (22.7% overall; 9.1% grade ≥3) and aspartate aminotransferase (22.7% overall; 6.1% grade ≥3).

Efficacy analysis showed a confirmed overall response rate of 72.0% and a disease control rate of 95.5% in the entire patient population, with 2.3% achieving a complete response (CR) and 69.7% achieving a partial response. The duration of response and progression free survival rate data remain immature, with 63.2% of responding patients still on treatment.

According to Dr. Ruiter, the primary analysis of the Beamion LUNG-1 Phase Ib Cohort 1 study confirms that zongertinib is well tolerated and effective in treating patients with HER2 m+ NSCLC.

"The promising efficacy and manageable safety profile support further development of zongertinib as a potential new therapy for this challenging patient population," she reported.

Provided by International Association for the Study of Lung Cancer